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### Authors

Son, Mary Beth F  
Gauvreau, Kimberlee  
Tremoulet, Adriana H  
et al.

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# Risk Model Development and Validation for Prediction of Coronary Artery Aneurysms in Kawasaki Disease in a North American Population

Mary Beth F. Son, MD; Kimberlee Gauvreau, ScD; Adriana H. Tremoulet, MD, MAS; Mindy Lo, MD, PhD; Annette L. Baker, RN, MSN, PNP; Sarah de Ferranti, MD, MPH; Fatma Dedeoglu, MD; Robert P. Sundel, MD; Kevin G. Friedman, MD; Jane C. Burns, MD; Jane W. Newburger, MD, MPH

**Background**—Accurate prediction of coronary artery aneurysms (CAAs) in patients with Kawasaki disease remains challenging in North American cohorts. We sought to develop and validate a risk model for CAA prediction.

**Methods and Results**—A binary outcome of CAA was defined as left anterior descending or right coronary artery Z score  $\geq 2.5$  at 2 to 8 weeks after fever onset in a development cohort (n=903) and a validation cohort (n=185) of patients with Kawasaki disease. Associations of baseline clinical, laboratory, and echocardiographic variables with later CAA were assessed in the development cohort using logistic regression. Discrimination (c statistic) and calibration (Hosmer-Lemeshow) of the final model were evaluated. A practical risk score assigning points to each variable in the final model was created based on model coefficients from the development cohort. Predictors of CAAs at 2 to 8 weeks were baseline Z score of left anterior descending or right coronary artery  $\geq 2.0$ , age  $< 6$  months, Asian race, and C-reactive protein  $\geq 13$  mg/dL (c=0.82 in the development cohort, c=0.93 in the validation cohort). The CAA risk score assigned 2 points for baseline Z score of left anterior descending or right coronary artery  $\geq 2.0$  and 1 point for each of the other variables, with creation of low- (0–1), moderate- (2), and high- (3–5) risk groups. The odds of CAAs were 16-fold greater in the high- versus the low-risk groups in the development cohort (odds ratio, 16.4; 95% CI, 9.71–27.7 [ $P<0.001$ ]), and  $>40$ -fold greater in the validation cohort (odds ratio, 44.0; 95% CI, 10.8–180 [ $P<0.001$ ]).

**Conclusions**—Our risk model for CAA in Kawasaki disease consisting of baseline demographic, laboratory, and echocardiographic variables had excellent predictive utility and should undergo prospective testing. (*J Am Heart Assoc.* 2019;8:e011319. DOI: 10.1161/JAHA.118.011319.)

**Key Words:** coronary aneurysm • echocardiography • Kawasaki disease • risk score

Kawasaki disease (KD) is the leading cause of acquired pediatric heart disease in developed nations. Treatment with intravenous immunoglobulin (IVIG) reduces the risk of coronary artery aneurysms (CAAs), a potentially devastating long-term complication of KD, by 5-fold.<sup>1</sup> The clinical window in which to diagnose and treat KD and thereby prevent long-term sequelae is brief, as children with KD should be treated within 10 days of fever onset. Accordingly, early identification of children who are at high risk for CAA is paramount, yet

instruments for such identification have remained elusive in non-Japanese populations. We previously assessed the clinical utility of established Japanese risk scores for predicting CAA development in a Western population and found them to be poorly predictive.<sup>2</sup> In contrast, coronary artery dimensions adjusted for body surface area (Z scores) at first diagnosis of KD, ie, baseline Z scores, were the most predictive risk factor for later CAA. In this study, we sought to create a risk model for CAA prediction with development and validation cohorts

From the Division of Immunology (M.B.F.S., M.L., F.D., R.P.S.) and Department of Cardiology (K.G., A.L.B., S.d.F., K.G.F., J.W.N.), Boston Children's Hospital, Boston, MA; Department of Pediatrics, Harvard Medical School, Boston, MA (M.B.F.S., M.L., S.d.F., F.D., R.P.S., K.G.F., J.W.N.); Department of Pediatrics, University of California San Diego School of Medicine, La Jolla, CA (A.H.T., J.C.B.); Department of Pediatrics, Rady Children's Hospital San Diego, San Diego, USA (A.H.T., J.C.B.).

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**Correspondence to:** Mary Beth F. Son, MD, Boston Children's Hospital, 300 Longwood Avenue, Boston, MA 02115. E-mail: marybeth.son@childrens.harvard.edu

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## Clinical Perspective

### What Is New?

- We developed and validated a practical risk score composed of baseline demographic, laboratory, and echocardiographic variables that has high predictive utility for future development of coronary artery aneurysms in patients with Kawasaki disease.

### What Are the Clinical Implications?

- An instrument to stratify risk of future coronary artery aneurysms in patients who present with acute Kawasaki disease provides the opportunity to intensify primary therapy and for closer echocardiographic surveillance.

(VCs), considering baseline Z score as well as other clinical and laboratory variables previously demonstrated to be predictive of worse outcomes in KD.

## Methods

Permission to use the validation data set was obtained from the Ancillary Studies Committee of the Pediatric Heart Network. This data set has since been made publicly available by the Pediatric Heart Network.<sup>3</sup> Data from the development cohort (DC) is not available because of privacy concerns.

## Development Cohort

The development data set for risk score creation was constituted from retrospective review of consecutive patients treated for KD at 2 academic centers. Specifically, we included all pediatric patients with KD (maximum age <19 years) treated at Boston Children's Hospital from January 2006 to May 2014 and at Rady Children's Hospital from July 1989 to May 2014. Patients were diagnosed with either complete KD (fever for  $\geq 4$  days [rarely  $\geq 3$  days] and  $\geq 4$  classical criteria for KD) or incomplete KD (<4 criteria with compatible laboratory and/or echocardiographic findings).<sup>1</sup> All patients were treated with IVIG and aspirin between days 3 through 10 of illness, with day 1 defined as the first day of fever. Patients were excluded if they: (1) had been transferred to either center for a second opinion, (2) had a prior episode of KD, (3) lacked laboratory data before 10 days of illness, (4) had laboratory examinations performed  $\geq 1$  day after IVIG administration, or (5) lacked echocardiographic data either at baseline (pre-IVIG or <2 days after IVIG administration) or within 2 to 8 weeks of illness. If a patient had >1 echocardiogram within 2 to 8 weeks after fever onset, we used the study that had the largest left anterior descending (LAD) artery and right coronary artery (RCA) measurements from the

time period. Approvals from institutional review boards with waivers of informed consent were obtained for this project.

## Validation Cohort

The VC was assembled during a National Heart, Lung, and Blood Institute Pediatric Heart Network clinical trial at 8 North American centers, which assessed the role of intravenous methylprednisolone in the primary treatment of KD.<sup>4</sup> Participants in the trial had been well characterized with respect to demographic, laboratory, and echocardiographic data. Because of the trial design, CAA as the outcome was assessed specifically at 5 weeks (window day 28 through day 42) after randomization. All exclusion criteria applied to the DC were applied to the VC.

## Data Obtained

We extracted demographic data, KD criteria, other medical variables, and laboratory data from electronic medical records and clinical databases, and from a deidentified research database for the validation data set. The following variables were assessed in the risk model: demographic factors, including age, sex, race, ethnicity, and incomplete versus complete criteria for KD; clinical factors including days of fever at diagnosis and need for treatment beyond 1 dose of IVIG (termed IVIG resistance); and baseline laboratory studies including white blood cell count, neutrophil count, hemoglobin, hematocrit, platelets, C-reactive protein (CRP), sodium, aspartate aminotransferase, alanine aminotransferase, albumin, and total bilirubin. Race and ethnicity were included as variables because prior studies have indicated that patients of Asian descent<sup>5,6</sup> or Hispanic ethnicity<sup>6</sup> are at increased risk for poor coronary outcomes.<sup>6</sup>

Echocardiographic data were collected from reports produced at the time of the study. Using the reported measurements of the LAD artery and RCA, Z scores for the proximal LAD artery and proximal RCA were calculated using Z score equations derived from previously described normative data.<sup>7</sup> Prior studies from our institution have shown high interobserver and intraobserver reliability for proximal LAD artery and RCA measurement.<sup>8,9</sup> The maximum Z score at baseline was defined as the larger of the proximal LAD artery and the proximal RCA Z scores. Children were classified as having the outcome of CAA if they had a Z score  $\geq 2.5$  in either the LAD artery or RCA between 2 and 8 weeks after illness onset.

## Statistical Analyses

Continuous variables are summarized as median with interquartile range or range, as noted, or as mean with SD. Categorical variables are summarized with frequencies and

percentages. In the DC, associations of baseline clinical, laboratory, and echocardiographic measurements with the binary outcome of CAA within 2 to 8 weeks of fever onset were assessed using Fisher exact test for categorical variables and the Wilcoxon rank sum test or unpaired *t* test for continuous variables. The ability of each measurement to discriminate between patients who did and did not develop CAA within 2 to 8 weeks was quantified using the *c* statistic.

Variables with  $P < 0.20$  in unadjusted analyses were considered for inclusion in a multivariable model. Multivariable logistic regression was performed using forward stepwise selection. Cut points were considered for continuous risk factors; the cut point resulting in the highest *c* statistic was chosen. Only variables that were both statistically significant at the 0.05 level by the likelihood ratio test and that improved the *c* statistic were retained in the final multivariable model. Goodness-of-fit of the model was assessed using the Hosmer-Lemeshow test. The multivariable model derived in the DC was then applied to the VC; discrimination of the model was evaluated by the *c* statistic, and goodness-of-fit by the Hosmer-Lemeshow test.

To calculate a risk score for each patient, the coefficients from the final multivariable logistic regression model in the DC were used to assign point values for each covariate in the model and the points were then summed for each patient. Higher scores indicated a greater number of risk factors and therefore higher presumed risk of CAA within 2 to 8 weeks of fever onset. The risk scores were used to define low-, moderate-, and high-risk categories, and risk category was used as the predictor in logistic regression models with the outcome of CAA within 2 to 8 weeks of fever onset for both the DC and the VC.

## Results

The DC consisted of 903 patients with KD (300 patients from Boston Children's Hospital and 603 patients from the University of California at San Diego), and the VC had 185 patients with KD. There was no overlap of patients between the 2 cohorts. The cohorts differed in regards to race, ethnicity, and number of clinical criteria for KD at diagnosis, but did not differ significantly in other baseline demographic or clinical variables (Table 1). Baseline laboratory studies and echocardiographic measurements were also similar between cohorts with the exception of hemoglobin, albumin, and baseline RCA Z score (Table 2). In the DC, the median time from fever onset to baseline echocardiogram was 6 days [interquartile range, 5–8]. The median time between baseline and outcome echocardiograms was 25 days [interquartile range, 14–37]. The percentage of patients with CAA was similar between the cohorts: 13.0% ( $n=117$ ) in the DC and 13.5% ( $n=25$ ) in the VC.

**Table 1.** Demographic and Clinical Characteristics of the DC and VC

Characteristic	DC (n=903) No. (%) or Median (Range)	VC (n=185) No. (%) or Median (Range)	P Value
Age at fever onset, y	2.8 (0.1–15.5)	3.0 (0.2–12.3)	0.912
Male sex	566 (63)	115 (62)	0.934
Race			
White	530 (60)	105 (57)	<0.001
Black	55 (6)	37 (20)	
Asian	139 (16)	26 (14)	
Other	18 (2)	4 (2)	
>1 race reported	143 (16)	12 (7)	
Any Asian race reported*	202 (22)	31 (17)	0.095
Hispanic	244 (27)	29 (16)	0.001
No. of clinical criteria reported			
≤3	147 (17)	7 (4)	<0.001
4	520 (59)	119 (64)	
5	208 (24)	59 (32)	
Days of fever at diagnosis	6 (3–10)	6 (4–10)	0.007
IVIG retreatment	141 (16)	24 (13)	0.431
CAAs at 2 to 8 wk after illness onset	117 (13)	25 (13.5) <sup>†</sup>	0.811
Small CAAs (Z score ≥2.5–5)	75 (8)	19 (10)	
Medium CAAs (Z score ≥5 to ≤10)	14 (2)	4 (2)	
Large or giant CAAs (Z score ≥10 or absolute dimension ≥8 mm)	28 (3)	2 (1)	

CAAs indicates coronary artery aneurysms; DC, development cohort; IVIG, intravenous immunoglobulin; VC, validation cohort.

\*One or both parents report Asian descent.

<sup>†</sup>As measured at 5 weeks, per Pediatric Heart Network trial protocol.

We first analyzed univariate associations between baseline variables and presence of CAA at 2 to 8 weeks after illness onset in the DC. The outcome of CAA was highly associated with younger age at fever onset; Asian race (one or both parents of Asian descent); higher white blood cell count and CRP; lower hemoglobin, hematocrit, and albumin; and maximum Z score at baseline of the RCA or LAD artery ( $\geq 2.00$ ) (Table 3).

For the multivariable model, independent predictors included maximum Z score at baseline  $\geq 2.00$ , age at fever onset  $< 6$  months, Asian race, and CRP  $\geq 13$  mg/dL. The model had a *c* statistic of 0.82 (Hosmer-Lemeshow,  $P=0.816$ ). Application of the multivariable model created in the

**Table 2.** Baseline Laboratory and Echocardiography Studies of DC and VC

Characteristic	DC (n=903)	VC (n=185)	P Value
Laboratory studies: median (interquartile range)			
White blood cell count, cells $\times 10^3/\text{mm}^3$	13.5 (10.5–17.3)	13.3 (10.1–16.6)	0.406
Neutrophils, %	59 (47–71)	61 (41–71)	0.328
Hemoglobin, g/dL	11.1 (10.4–11.8)	10.9 (10.1–11.7)	0.047
Hematocrit, %	32.4 (30.7–34.5)	32.0 (30.0–34.0)	0.066
Platelets, cells $\times 10^3/\text{mm}^3$	366 (287–457)	389 (303–464)	0.190
CRP, mg/dL	7.9 (4.5–15.2)	7.2 (4.0–15.3)	0.295
Sodium—mmol/L	135 (133–137)	NA	
AST, U/L	36 (26–55)	NA	
ALT, U/L	38 (19–103)	32 (16–84)	0.062
Albumin, g/dL	3.6 (3.2–4.0)	3.3 (2.8–3.7)	<0.001
Total bilirubin, mg/dL	0.3 (0.2–0.7)	NA	
Baseline echocardiography, mean $\pm$ SD			
RCA Z score	0.94 $\pm$ 1.37	1.21 $\pm$ 1.39	0.019
LAD artery Z score	1.18 $\pm$ 1.66	1.13 $\pm$ 1.55	0.665
Maximum Z score of the LAD artery and RCA	1.61 $\pm$ 1.59	1.69 $\pm$ 1.50	0.503
RCA Z score			
$\geq 2.00$	148 (16)	36 (20)	0.277
$\geq 2.50$	88 (10)	26 (14)	0.083
$\geq 3.00$	57 (6)	15 (8)	0.327
LAD artery Z score			
$\geq 2.00$	195 (22)	40 (22)	1.000
$\geq 2.50$	122 (14)	29 (16)	0.415
$\geq 3.00$	76 (8)	17 (9)	0.772
Maximum baseline Z score			
$\geq 2.00$	264 (29)	55 (30)	0.929
$\geq 2.50$	170 (19)	42 (23)	0.223
$\geq 3.00$	110 (12)	27 (15)	0.394
Baseline CAAs			
Small CAAs (Z score $\geq 2.5$ –5)	149 (16)	38 (21)	0.394
Medium CAAs (Z score $\geq 5$ to $\leq 10$ )	15 (2)	4 (2)	
Large or giant CAAs (Z score $\geq 10$ or absolute dimension $\geq 8$ mm)	6 (1)	0 (0)	

ALT indicates alanine aminotransferase; AST, aspartate aminotransferase; CAAs, coronary artery aneurysms; CRP, C-reactive protein; DC, development cohort; LAD, left anterior descending; NA, not available; RCA, right coronary artery; VC, validation cohort.

development data set to the VC revealed a c statistic of 0.93 (Hosmer-Lemeshow,  $P=0.211$ ), but only the maximum Z score at baseline was statistically significant.

Using the demographic and clinical characteristics yielded by the logistic regression, a simple scoring model was constructed in the DC. For each patient, 2 points were assigned if the maximum Z score at baseline was  $\geq 2.00$ , 1 point if age at fever onset was  $<6$  months, 1 point if Asian

race was reported, and 1 point if baseline CRP was  $\geq 13$  mg/dL. A 3-tier scoring system was determined based on the sum of points per patient: 0 to 1 point (low risk), 2 points (moderate risk), and 3 to 5 points (high risk). Patients in the DC and VC had a similar distribution of numeric values (0–5 points) for the risk score (Table 4). In the DC, 16.4% of patients had high-risk scores (numeric values from 3 to 5), and 41.2% of these patients had CAAs at 2 to 8 weeks after fever onset. Similarly,

**Table 3.** Associations With CAAs in the DC

Univariate Associations in DC With CAAs (n=117, 13.0%)		
Characteristic	Odds Ratio (95% CI)	P Value
Age at fever onset <6 mo	3.71 (2.06–6.68)	<0.001
Asian race reported	2.29 (1.51–3.47)	<0.001
Days of fever (↑ 1 d)	1.11 (0.99–1.23)	0.063
Maximum Z score at baseline (↑ 1 Z score unit)	2.35 (1.97–2.79)	<0.001
Maximum Z score at baseline ≥2.00	9.01 (5.81–14.0)	<0.001
White blood cell count ≥16 cells/mm <sup>3</sup>	2.43 (1.64–3.61)	<0.001
Hemoglobin <10.3 g/dL	1.98 (1.28–3.05)	0.002
Hematocrit <32	2.19 (1.47–3.27)	<0.001
CRP ≥13 mg/dL	2.13 (1.41–3.21)	<0.001
Albumin <3.2 g/dL	3.63 (2.23–5.92)	<0.001
Final multivariable model: c statistic=0.82 (Hosmer-Lemeshow, P=0.816)		
Maximum Z score at baseline ≥2.00	9.82 (6.09–15.9)	<0.001
Age at fever onset <6 mo	3.02 (1.5–6.06)	0.002
Any Asian race reported	1.95 (1.2–3.17)	0.007
CRP ≥13 mg/dL	2.06 (1.3–3.26)	0.002

CAAs indicates coronary artery aneurysms; CRP, C-reactive protein; DC, development cohort.

12.4% of the VC had risk scores from 3 to 5, and over half of these patients (52.2%) had CAA. Compared with patients who had a risk score of 0 to 1, those whose risk score was ≥3 in the DC had a much higher risk of having CAAs (odds ratio, 16.4; 95% CI, 9.71–27.7 [ $P<0.001$ ]) (Table 5). The odds of having CAA in those with a risk score of 2 versus 0 to 1 was also higher (odds ratio, 5.4; 95% CI, 3.09–9.5 [ $P<0.001$ ]). Analysis of the risk score in the VC revealed that the high-risk group had a very high odds ratio of CAA as compared with the low-risk group (odds ratio, 44.0; 95% CI, 10.8–180 [ $P<0.001$ ]). However, the CIs were widened by the low prevalence outcome, with only 3 patients with CAAs in the low-risk group in the VC. The c statistic for the risk score in the DC was 0.79 (Hosmer-Lemeshow,  $P=0.999$ ). When the risk score was applied to the VC, the c statistic rose to 0.85 (Hosmer-Lemeshow,  $P=0.999$ ).

## Discussion

Although the majority of children with KD have excellent clinical outcomes after treatment with a single dose of IVIG in the first 10 days of illness, ≈25% of children and >50% of infants younger than 6 months with KD have Z scores ≥2.5 in the first 12 weeks of illness in both North American and Japanese populations.<sup>7,10–12</sup> Approximately 1% of patients

**Table 4.** Risk Score\* in the DC and VC

Risk Score	No. (%)	No. (%) With CAA
DC (n=903)		
0	346 (38)	24 (4.1)
1	239 (26)	
2	170 (19)	32 (18.8)
3	108 (12)	
4	36 (4)	
5	4 (<1)	61 (41.2)
VC (n=185)		
0	79 (43)	3 (2.4)
1	45 (24)	
2	38 (21)	10 (26.3)
3	18 (10)	
4	5 (3)	
5	0 (0)	12 (52.2)

CAAs indicates coronary artery aneurysm; DC, development cohort; VC, validation cohort.

\*Risk scoring: 2 points if maximum baseline Z score ≥2.00, 1 point if age at fever onset younger than 6 months, 1 point if Asian race reported, 1 point if C-reactive protein ≥13 mg/dL.

with KD progress to giant aneurysms that can cause ischemic heart disease, including angina, myocardial infarction, and sudden death. Adjuvant immunomodulatory therapies, administered together with standard IVIG, may further lower the incidence of CAA. To institute such therapies early enough to prevent damage of the coronary arterial wall, high-risk children must be identified at the time of diagnosis. Tools for risk stratification of patients with KD at presentation have proven elusive, however. A prior risk score created in North America included presence of fever following IVIG administration,<sup>13</sup> which is less helpful in determining at diagnosis who would benefit from intensification of initial treatment. There are several Japanese risk-scoring systems for predicting IVIG resistance, which is highly associated with CAA, using different clinical and laboratory values. The Kobayashi score

**Table 5.** Three-Tier Risk Score

Risk Score (vs 0–1)	Odds Ratio	95% CI	P Value
Three-tier risk model in the DC (c statistic=0.79)			
2 (moderate risk)	5.42	3.09–9.50	<0.001
3 to 5 (high risk)	16.4	9.71–27.7	<0.001
Three-tier risk model in the VC (c statistic=0.85)			
2 (moderate risk)	14.4	3.72–55.8	<0.001
3 to 5 (high risk)	44.0	10.8–180	<0.001

DC indicates development cohort; VC, validation cohort.



is now widely used in Japanese populations to stratify risk for IVIG resistance and consists of easily accessible demographic and laboratory values.<sup>14</sup> Unfortunately, the Kobayashi score did not accurately predict poor outcomes in non-Japanese populations.<sup>2,15</sup> Similarly, the other Japanese risk scores have demonstrated good specificity but low sensitivity for predicting IVIG resistance or CAA in North American children.<sup>15,16</sup> In contrast, baseline echocardiographic measurements have shown promise for predicting CAA.<sup>2,7,17</sup> We sought to develop and validate a risk score for CAA in a North American population of patients with KD using patient, laboratory, and echocardiographic factors assessed at the time of presentation.

In our development data set, we found that a baseline maximum Z score of the LAD artery or RCA  $\geq 2$ , age at fever onset of younger than 6 months, Asian race, and CRP  $\geq 13$  mg/dL at diagnosis were independent risk factors for CAA in a multivariable regression analysis and yielded a c statistic of 0.82. Each of these factors has been previously associated with increased risk for IVIG resistance or CAA in North American populations.<sup>1,2,18–20</sup> The finding that age younger than 6 months is highly predictive of CAA has been recently demonstrated by Salgado et al.<sup>12</sup> In that study, 43% of infants younger than 6 months treated within the first 10 days of illness had dilated or aneurysmal coronary arteries at baseline, and 19% of those whose coronary arteries had normal dimensions at presentation went on to develop dilated or aneurysmal coronary arteries within 8 weeks of diagnosis. This finding underscores the importance of heightened vigilance for KD in very young infants with prolonged fever, even in the absence of diagnostic criteria.<sup>1</sup> Asian race is not only a risk factor for KD itself<sup>6,19</sup> but also for a higher rate of CAA.<sup>1,5,20</sup> Of note, we classified children as Asian if they selected it as the sole race or if they were of mixed Asian race (ie,  $>1$  race). We did not have further detailed information regarding Asian race in either cohort (ie, South Asian versus East Asian). In a retrospective study of coronary outcomes in North America and Japan, Ogata and colleagues<sup>11</sup> found that when adjusting for age, sex, and treatment response, Japanese race was associated with having a higher maximum Z score of the LAD artery or RCA within the first 12 weeks of illness. To our knowledge, there are no other studies that directly compare coronary artery outcomes in Asians versus non-Asians using standardized definitions. CRP has consistently been found to be elevated in patients with KD and is a component in the Kobayashi, Sano, and Egami risk scores for prediction of IVIG resistance.<sup>14,21,22</sup> In a recent study in a Korean population, elevated CRP predicted both IVIG resistance as well as coronary artery abnormalities.<sup>23</sup> Furthermore, CRP was noted to be higher in a North American population of children who developed IVIG resistance.<sup>24</sup> Given our prior assessment of Japanese risk scores in North American

populations,<sup>2</sup> we applied the Kobayashi, Egami, Sano, and Harada risk scores to the DC and found c statistics ranging from 0.54 to 0.61, which is commensurate with our prior findings and far less predictive than our current model (c statistic, 0.82).

Application of the multivariable model derived in the DC to the VC yielded a c statistic of 0.93. In the VC, the baseline Z score had the highest discrimination in the model, consistent with prior studies underscoring the importance of baseline echocardiographic measurements. We also devised a 3-tier risk scoring system with high predictive utility using the variables identified in the regression analysis to provide a practical tool for early identification of patients at risk for CAA. An advantage of our risk score is the easy accessibility of the component variables at the time of KD presentation. As we selected variables available at diagnosis, we did not include differences in treatment regimens in our analysis. Demographic risk factors are known at diagnosis, and collection of laboratory values, such as CRP, as well as baseline echocardiography, are the standard of care in KD. If the risk score from the current study proves predictive in other populations, it could be useful not only in tailoring primary treatment of KD in children to their risk of CAA, but also in providing a means of selecting high-risk children for participation in clinical trials of intensified primary therapy. Of note, the optimal adjunctive anti-inflammatory agent(s) used together with IVIG in the primary treatment of high-risk KD is controversial, with practice variation among practitioners and centers.<sup>1,25,26</sup> Last, patients who are identified as high risk per our score may benefit from frequent (eg, twice weekly) echocardiography during the initial illness until coronary dimensions stabilize to detect abnormalities early enough to treat more aggressively with immunosuppressive therapies.

## Study Limitations

Our analyses were limited by the differences in data collection between the DC and the VC. Data collection in the former was part of routine clinical care, whereas data in the latter were collected prospectively in the setting of a multicenter clinical trial. The differences between the 2 cohorts in race, ethnicity, and number of clinical criteria at diagnosis were likely the result of regional differences in the populations and differences in treatment of patients with KD in a real-world setting compared with a clinical trial, which uses strictly defined selection criteria. Differences between the cohorts in laboratory values (hemoglobin and albumin) and baseline RCA Z score may be caused by the smaller number of patients in the VC. Differences between the cohorts in laboratory values (hemoglobin and albumin) and baseline RCA Z score may be attributable to the smaller number of patients in the VC. Neither hemoglobin nor albumin were components in the

multivariable model or risk score. The cohorts had similar baseline maximum Z score, the echocardiographic variable in the risk model. Thus, we do not believe these differences in laboratory values and baseline RCA Z scores were likely to have had an important influence on the analysis. Both the development and validation data sets were obtained in a select group of academic medical centers with expertise in KD. Although our risk score was developed based on echocardiographic findings in the range of 2 to 8 weeks after illness onset, it performed well in the VC, in whom the score was tested on echocardiograms performed 28 to 42 days of illness ( $\approx 5$  weeks). Importantly, in our risk score model,  $\approx 2\%$  to  $4\%$  of children with a risk score of 0 had CAA, highlighting that the risk score should not supplant clinician judgment in individual patients. Finally, the risk score is designed for assessment of patients with KD at the time of presentation; risk after presentation should be assessed serially and therapies adjusted accordingly, as reviewed in the 2017 American Heart Association KD guidelines.

## Conclusions

We developed and validated a risk score to predict the occurrence of CAA within the first 2 to 8 weeks of illness using 2 North American cohorts of patients with KD. We found that data obtained routinely at diagnosis, including age, race, CRP, and coronary artery measurements from baseline echocardiography, were independently associated with CAA. Our simple scoring method to delineate 3 groups of children with KD at low, moderate, and high risk of having CAA at 2 to 8 weeks after illness onset may be a helpful tool to guide adjunctive anti-inflammatory therapies for primary treatment and frequency of echocardiographic follow-up. Future studies should test this risk score in larger and more diverse care settings in North America to assess accuracy and generalizability.

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## Disclosures

None.

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